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# Success and Outcomes Following a Second Salvage Attempt for Free Flap Compromise in Patients Undergoing Head and Neck Reconstruction

Allison A. Slijepcevic, MD; Gavin Young, MS; Justin Shinn, MD; Steven B. Cannady, MD; Matthew Hanasono, MD; Matthew Old, MD; Jeewanjot S. Grewal, MD; Tamer Ghanem, MD, PhD; Yadranko Ducic, MD; Joseph M. Curry, MD; Mark K. Wax, MD

**IMPORTANCE** Incidence of perioperative free flap compromise is low, with successful salvage in up to 70%. When the flap is compromised a second time, the value of intervening is unknown.

**OBJECTIVE** To assess the outcomes of a second revascularization attempt for compromised free flaps.

**DESIGN, SETTING, AND PARTICIPANTS** This multicenter retrospective medical record review included patients undergoing head and neck reconstruction with free flaps at 6 US medical centers from January 1, 2000, through December 30, 2020. Patients were 18 years or older with a history of head and neck defects from cancer, osteoradionecrosis, or other wounds. Of 3510 flaps identified, 79 were successfully salvaged once, became compromised a second time, and underwent attempted salvage.

**MAIN OUTCOME AND MEASURE** Flaps with a history of initial compromise and successful revascularization demonstrating second episodes of compromise followed by second salvage attempts.

**RESULTS** A total of 79 patients (mean age, 64 years; 61 [77%] men) were included in the analysis. Of the 79 flaps undergoing second salvage attempts, 24 (30%) survived while 55 (70%) demonstrated necrosis. Arterial or venous thrombectomy was performed in 17 of the 24 (71%) flaps that survived and 23 of the 55 (42%) flaps demonstrating necrosis (odds ratio, 3.38; 95% CI, 1.21-9.47). When venous compromise was encountered, changing the anastomotic vein was associated with decreased survival compared with not changing the vein (29 of 55 [53%] flaps vs 10 of 24 [42%] flaps); vein revision to an alternative branch was completed in 1 of the 24 (4%) flaps that survived and 19 of the 55 (35%) flaps with necrosis (odds ratio, 0.08; 95% CI, 0.00-0.60). Factors that were not associated with flap survival following second salvage attempts included flap type, cause of flap failure, postoperative complications, patient comorbidities, and heparin administration after second salvage.

**CONCLUSIONS AND RELEVANCE** In this cohort study, second salvage was successful in 30% of free flaps. Flaps that underwent arterial or venous thrombectomy demonstrated better survival, while vein revision to neighboring branch veins was associated with worse flap outcomes.

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Functional rehabilitation following composite ablative procedures in the head and neck may be reconstructed with composite free tissue grafts. Free tissue transfer has the potential to provide reliable results; however, vascular compromise in the perioperative period can occur in up to 10% to 15% of cases. Surgical salvage of compromised free flaps provides revascularization in up to 60% to 80% of patients.<sup>1-3</sup>

While the initial salvage rate of compromised free flaps demonstrates a high measure of success, there exists a small number of flaps that will develop vascular compromise a second time. In these cases, the rate of a second successful revascularization is unknown.<sup>1,4,5</sup>

This cohort study aims to determine the outcomes following the salvage of free flaps demonstrating a second episode of compromise following prior successful revascularization. Additionally, the factors associated with success and failure of second salvage attempts are investigated.

## Methods

### Data Collection

This study is a multicenter retrospective review. Data were collected between January 1, 2000, and December 30, 2020, through medical record review at Oregon Health & Science University, University of Pennsylvania, The University of Texas MD Anderson Cancer Center, The Ohio State University, Henry Ford Health System in Michigan, and the Head & Neck Cancer Center of Texas. Patients were 18 years and older with a history of head and neck defects from cancer, osteoradionecrosis, or other wounds that were reconstructed with free flaps that demonstrated a history of flap compromise with successful initial salvage that then underwent a second episode of flap compromise treated with surgical intervention. The institutional review board at Oregon Health & Science University approved this study and waived the need for patient informed consent owing to use of deidentified data.

Independent variables, including patient demographics, medical history, site of head and neck cancer, surgical ablation, flap reconstruction, and flap vascular anastomosis, were defined based on medical record review documentation and captured by medical record review completed by all authors. At Oregon Health & Science University, intravenous heparin administration was titrated to a standardized stroke protocol goal partial thromboplastin time of 65 seconds. Dependent variables, including cause of flap compromise, use of perioperative heparin, management of flap death, and postoperative complications, were also collected by all authors during medical record review. The cause of the second episode of flap compromise was obtained from operative and postoperative notes during the medical record review. The cause of flap failure was validated by the individual authors who contributed data from different institutions; given the small number of medical records from each data collection site, individual authors were independently responsible for data collection.

### Statistical Analysis

Odds ratios (ORs) and 95% CIs for categorical variables were calculated using R statistical software, version 4.1.2

## Key Points

**Question** What is the outcome of free flaps in patients undergoing head and neck reconstruction with a history of initial flap failure and successful revascularization demonstrating second episodes of flap compromise treated with surgical intervention?

**Findings** In this cohort study of 79 patients with flaps undergoing second salvage attempts, approximately 1 in 3 flaps survived. Flaps undergoing thrombectomy demonstrated improved survival, while flaps with venous compromise demonstrated lower rates of survival.

**Meaning** Flaps demonstrating arterial or venous thrombi that are amenable to thrombectomy may have increased rates of survival following second salvage.

(R Foundation). Odds ratios for each category of cancer subsite, surgical indication, flap type, cause of flap failure, artery anastomosis revision, and vein anastomosis revision were calculated compared with the reference proportions of oral cavity/maxilla/mandible, trauma, anterolateral thigh, unknown cause, facial artery, and facial vein, respectively.

## Results

A total of 3510 free flaps were completed during the study period. Of these, the flaps of 79 patients demonstrated a second episode of compromise followed by a second attempt at surgical revascularization.

The mean patient age was 64 years. Of the 79 patients, 61 (77%) were men, 18 (23%) were women, and 58 (73%) were former or current smokers. Reported comorbidities included cardiac disease (n = 24 [30%]) and diabetes (n = 17 [22%]). Prior radiation therapy was received by 31 (39%) patients, and prior chemotherapy was received by 22 (28%).

The most common indications for surgery and free flap reconstruction included malignant tumor (n = 60 [76%]) and osteoradionecrosis (n = 11 [14%]). **Table 1** summarizes the indications for initial surgeries. The main subsites of cancer included the oral cavity (n = 35 [44%]), mandible (n = 11 [14%]), and oropharynx (n = 8 [10%]). **Table 2** summarizes the subsites of cancer.

Flap donor sites included radial forearm (n = 22 [28%]), anterolateral thigh (n = 19 [24%]), fibula (n = 18 [23%]), scapula (n = 9 [11%]), latissimus dorsi (n = 8 [10%]), and other (n = 3 [4%]). The most common causes of initial flap compromise included venous thrombosis (n = 43 [54%]), arterial thrombosis (n = 22 [28%]), both arterial and venous thrombosis (n = 6 [8%]), unknown causes (n = 6 [8%]), and infection (n = 2 [3%]). The most common causes of the second episode of flap compromise included venous thrombosis (n = 24 [30%]), both arterial and venous thrombosis (n = 24 [30%]), unknown causes (n = 15 [19%]), arterial thrombosis (n = 14 [18%]), and infection (n = 2 [3%]).

**Table 2** summarizes factors associated with flap survival following second salvage. Following second salvage attempts, 24 (30%) flaps survived and 55 (70%) flaps showed necrosis. Arterial compromise was reported in 7 of the 24 (29%)

**Table 1. Indications for Surgical Reconstruction With Free Flaps, Subsites of Head and Neck Cancer, and Causes of Second Episodes of Flap Compromise (n = 79)**

Characteristic	No. (%)
Indication for surgery	
Cancer	60 (76)
Osteoradionecrosis	11 (14)
Other	4 (5)
Nonhealing wounds	3 (4)
Trauma	1 (1)
Subsites of head and neck cancer	
Oral cavity	35 (44)
Mandible	11 (14)
Oropharynx	8 (10)
Scalp	7 (9)
Larynx	6 (8)
Maxilla	6 (8)
Multiple sites	3 (4)
Other	2 (2)
Hypopharynx	1 (1)
Cause of second episodes of flap compromise	
Both venous and arterial thrombosis	24 (30)
Venous thrombosis	24 (30)
Unknown cause	15 (19)
Arterial thrombosis	14 (18)
Infection	2 (3)

flaps that survived and 7 of the 55 (13%) flaps with necrosis following second salvage. Arterial and/or venous thrombectomy was performed in 17 of the 24 (71%) flaps that survived and 23 of the 55 (42%) flaps with necrosis (OR, 3.38; 95% CI, 1.21-9.47). When venous compromise was encountered, changing the anastomotic vein was associated with decreased survival compared with not changing the vein (29 of 55 [53%] flaps vs 10 of 24 [42%] flaps); vein revision to an alternative branch was completed in 1 of the 24 (4%) flaps that survived and 19 of the 55 (35%) flaps with necrosis (OR, 0.08; 95% CI, 0.00-0.60).

Among the 79 patients, intravenous heparin was administered to 24 (30%) following initial successful salvages. Following second salvage procedures, 43 (54%) patients were receiving heparin, including 11 of the 24 (46%) patients with flaps demonstrating survival and 32 of the 55 (58%) patients with flaps demonstrating necrosis (OR, 1.37; 95% CI, 0.52-3.60).

Factors that were not associated with flap survival following second salvage attempts included patient demographics, comorbidities, and head and neck surgery. Patient sex (OR, 1.20; 95% CI, 0.39-3.77), history of cardiac disease (OR, 1.79; 95% CI, 0.40-7.52), history of smoking (OR, 1.09; 95% CI, 0.34-3.69), history of radiation therapy (OR, 1.74; 95% CI, 0.59-5.15), and postoperative complications (OR, 0.62; 95% CI, 0.21-1.82) were not associated with flap outcomes following second salvage.

The 55 flaps demonstrating necrosis following second salvage attempts were managed with several types of secondary

**Table 2. Flaps Demonstrating Survival Following Second Salvage Attempts and Variables Associated With Flap Survival**

Variable	Flap survival, No./total No. (%)	Odds ratio (95% CI)
Total	24/79 (30)	NA
Sex		
Female	6/18 (33)	1.20 (0.39-3.77)
Male	18/61 (30)	1 [Reference]
History of cardiac disease		
No	16/55 (29)	1.22 (0.44-3.40)
Yes	8/24 (33)	
History of diabetes		
No	19/62 (31)	0.94 (0.29-3.05)
Yes	5/17 (29)	
History of smoking		
None	7/24 (29)	1.09 (0.38-3.10)
Former/current	17/55 (31)	
Cancer subsite		
Oral cavity/maxilla/mandible	12/52 (23)	1 [Reference]
Scalp/multiple sites/other	5/12 (42)	2.38 (0.64-8.90)
Hypopharynx/oropharynx/larynx	7/15 (47)	2.90 (0.88-9.70)
Surgical indication		
Trauma	1/4 (25)	1 [Reference]
Cancer	18/60 (30)	1.30 (0.12-13.20)
Osteoradionecrosis	5/11 (45)	2.50 (0.19-32.20)
Flap type		
Anterolateral thigh	5/19 (26)	1 [Reference]
Fibula	5/18 (28)	1.08 (0.25-4.60)
Latissimus dorsi	3/8 (38)	1.68 (0.29-9.70)
History of radiation therapy		
No	12/47 (26)	1.74 (0.59-5.15)
Yes	12/32 (38)	
History of chemotherapy		
No	16/55 (29)	1.22 (0.37-3.78)
Yes	8/24 (33)	
Cause of flap failure		
Infection	0/2 (0)	∞
Arterial and venous thrombosis	7/24 (29)	1 [Reference]
Venous thrombosis	9/24 (38)	1.46 (0.44-4.90)
Arterial thrombosis	7/14 (50)	2.43 (0.62-9.50)
Unknown	1/15 (7)	0.17 (0.02-1.60)
Artery anastomosis revision		
Not revised	6/19 (32)	1 [Reference]
Facial artery	1/6 (17)	0.43 (0.04-4.60)
Other	5/21 (24)	0.68 (0.17-2.70)
Same revised	12/33 (36)	1.20 (0.37-4.10)
Vein anastomosis revision		
Not revised	6/21 (28)	1 [Reference]
Facial/other	1/20 (5)	0.13 (0.01-1.20)
Same revised	8/19 (42)	1.82 (0.49-6.80)
Internal jugular	9/19 (47)	2.25 (0.61-8.30)

(continued)

**Table 2. Flaps Demonstrating Survival Following Second Salvage Attempts and Variables Associated With Flap Survival (continued)**

Variable	Flap survival, No./total No. (%)	Odds ratio (95% CI)
Heparin administration		
No	13/47 (28)	1 [Reference]
Yes	11/32 (34)	1.37 (0.52-3.60)
Thrombectomy		
No	7/39 (18)	3.38 (1.21-9.47)
Yes	17/40 (42)	
Postoperative complications		
Yes	12/46 (26)	1.62 (0.62-4.26)
No	12/33 (36)	
Fistula		
Yes	1/11 (9)	5.11 (0.62-42.42)
No	23/68 (34)	
Hematoma		
Yes	5/24 (21)	2.00 (0.65-6.22)
No	19/55 (34)	
Wound dehiscence		
No	16/63 (25)	2.94 (0.95-9.11)
Yes	8/16 (50)	
Wound infection		
Yes	6/23 (26)	1.34 (0.45-3.98)
No	18/56 (32)	

Abbreviation: NA, not applicable.

reconstructions. Secondary reconstructions included second free flaps (n = 24 [44%]), regional flaps (n = 21 [38%]), other methods (n = 7 [13%]), and conservative care (n = 3 [5%]).

## Discussion

Free tissue transfer has been shown to be the best method of reconstructing composite defects with composite tissue. Wound healing by bringing in fresh, untreated tissue is best. Hospitalizations and patient morbidity are decreased. This, in turn, allows for the best rehabilitative potential. Vascular compromise in the immediate perioperative period is well recognized. Immediate return to the operating room allows for the best opportunities to salvage the flap. The majority of flaps can be salvaged, with rates of 60% to 80% reported.<sup>1-3</sup> Unfortunately, there exists a small number of patients whose flap will become compromised a second time, and they are returned to the operating room for a second attempt at salvage. The outcomes of free flaps undergoing multiple revisions for vascular compromise are unknown. Most of the literature on this subject is anecdotal, with no clear guidelines to assist in the management of these patients.

This study showed that one-third of patients undergoing second salvage procedures for free flap compromise achieved successful flap revascularization. Or, put another way, two-thirds of flaps were not salvageable.

A key aspect of free flap survival following second salvage attempts was the identification and management of arterial and/or venous thromboses in the flap pedicle. The present data suggest that if an identifiable anastomotic clot is the source of flap compromise, particularly in the arterial system, surgical revision has a greater chance of success when compared with flaps without an isolated identifiable intravascular pathology. Arterial thrombi are associated with less severe metabolic abnormalities when compared with the metabolic derangements associated with venous thrombi, which may account for the improved flap outcomes following arterial thrombectomy.<sup>6</sup> The present data contrast with a study by Chiu et al<sup>3</sup> that included 87 flaps used in primary head and neck reconstruction; flap failure was demonstrated in 58% of flaps with arterial thrombi and 31% of flaps with venous thrombi, suggesting arterial thromboses were associated with higher rates of flap compromise. In our experience, intravascular thrombi represent an isolated vascular issue that may be successfully resolved during revision surgery. In contrast, flaps with venous congestion and no identifiable thrombi may not have adequate circulation due to flap anatomy, and these flaps may remain nonviable despite multiple vein revisions.<sup>7</sup> Additionally, when comparing the causes of compromise of flaps demonstrating initial compromise and flaps demonstrating second episodes of compromise, higher rates of unknown causes of compromise are reported in flaps undergoing second salvage attempts, which may account for the low overall salvage rates following second salvage attempts.

The use of intravenous heparin in this study was not associated with increased flap success following second salvage surgeries. A diverse body of literature exists demonstrating equivocal flap outcomes with use of anticoagulation.<sup>3,5,8,9</sup> A meta-analysis by Pan et al<sup>8</sup> evidenced that high-dose anticoagulation was associated with increased rates of flap compromise. Administering heparin is a medical intervention that is often used anecdotally per surgeon experience. Heparin use may not be useful in flaps with technical errors at pedicle anastomosis site, recurrent kinking of the pedicle, or inadequate vasculature to support venous outflow. Additionally, heparin use has been associated with acute onset of hematomas at donor sites, necessitating urgent surgical intervention. A study by Numajiri et al<sup>10</sup> that included 121 patients undergoing head and neck oncologic ablation and free flap reconstruction with postoperative anticoagulation demonstrated that heparin administration did not improve flap outcomes and resulted in increased postoperative hemorrhages. The use of heparin remains at the discretion of individual surgeons, and the risk of postoperative complications from anticoagulation may not outweigh the unknown benefit to compromised flaps. It may also be that flaps undergoing salvage surgery for a second time may have an underlying flow problem that will not be resolved with surgical or medical intervention.

The present data demonstrated that flap type was not associated with flap outcomes in a specific population of patients with flaps having multiple episodes of compromise. While there is no immediate literature for comparison, prior literature suggests that osteocutaneous flaps, perforator flaps, and buried flaps demonstrate higher rates of compromise.<sup>1,11-13</sup>

Additionally, site of flap reconstruction was not shown to increase flap compromise in this study. This is in contrast to prior studies in head and neck literature showing that oral cavity and pharyngeal/laryngeal insets used in primary reconstruction are associated with increased rates of flap compromise.<sup>13</sup> The present study suggests that factors surrounding flap pedicle flow, including surgical technique and pedicle geometry, may have the greatest effect on flap outcomes following second salvage.

The data in this study showed that flap outcomes were not associated with medical comorbidities, smoking, or post-operative complications. Prior literature showed that a history of radiation therapy, smoking, and wound infection were associated with free flap compromise in primary reconstructions.<sup>14-17</sup> To our knowledge, there are no data regarding flap outcomes for secondary reconstructions. A systematic review by Herle et al<sup>15</sup> demonstrated increased rates of flap compromise and wound complications in patients with a history of radiation therapy; furthermore, higher doses of radiation were correlated with increased rates of flap failure. The present study shows that flap outcomes following second salvage procedures are not associated with underlying health factors and are instead dependent on flap physiology.

The findings from this study are intended to guide surgeons when deciding to proceed with second salvage attempts for compromised flaps. These data suggest that flaps with a history of identifiable pedicle thrombi are more likely to survive second salvage. Additionally, flaps with a history of arterial thrombi have greater likelihood of successful outcomes. Flaps with a history of inadequate venous outflow and no solitary identifiable intravascular thrombi are at risk for necrosis following second salvage. Overall, the rate of successful flap survival following second salvage is very low, and second salvage attempts may be reserved for patients unlikely to benefit from less optimal reconstructive procedures. The management of reconstruction sites following failed second salvage procedures often depends on the complexity of the reconstructive site, goals for aesthetics and function of the reconstruction, and patient health. The present data show that most surgeons chose to harvest a new free flap or use locoregional tissue to reconstruct prior flap sites. While the harvesting of a new free flap is associated with considerable morbidity,

it may provide an optimal reconstructive outcome for patients without underlying risk factors for flap compromise.

### Limitations

This study is limited by the small number of patients with flaps undergoing second salvage attempts. Another limitation is the failure to include a measure of the overall severity of comorbidity. Instead, we only captured the independent presence of 2 conditions: history of cardiac disease and diabetes. While this study presents novel data on the outcomes of second salvage attempts for flaps with prior failures, the decision on which flap to intervene on, when to use Doppler ultrasonography, and when to heparinize is not well documented. These are a few of the factors that may have influenced outcome measures. While a number of patient-related and surgical variables were assessed for association with flap success, additional factors may exist that were not captured in the medical record reviews. Additionally, of the 3510 flaps completed during this study period, the rate of first salvage attempts is unknown. While the literature reports initial flap salvage rates ranging from 60% to 80%, differences in the initial salvage rates in the present data may have presented a confounding bias in the data set; if the present rate of initial salvage was higher than rates in the literature, the second salvage rates may be falsely elevated.<sup>1-3</sup> However, based on the number of known flaps with a history of initial compromise (350 of 3510 [10%]), the initial flap salvage rate was 77% (270 of 350). This rate is comparable with reported salvage rates and suggests these data regarding second salvage rates may be accurate.

### Conclusions

In this cohort study, second salvage surgeries successfully perfused 30% of flaps. Thrombectomy of isolated thrombi was associated with flap success following second salvage surgeries. Flap failure associated with venous compromise demonstrated worse outcomes. Second salvage procedures may improve flap survival in a small number of patients with flaps compromised by pedicle thrombi and may be advantageous when secondary free flaps or locoregional flap reconstructions are not preferred.

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**Author Contributions:** Dr Slijepcevic had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

**Concept and design:** Cannady, Hanasono, Old, Ghanem, Curry, Wax.

**Acquisition, analysis, or interpretation of data:** Slijepcevic, Young, Shinn, Cannady, Grewal, Ghanem, Ducic, Curry, Wax.

**Drafting of the manuscript:** Slijepcevic, Ducic, Wax.  
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**Statistical analysis:** Young, Shinn, Grewal.  
**Administrative, technical, or material support:** Slijepcevic, Shinn, Cannady, Curry, Wax.  
**Supervision:** Cannady, Old, Ducic, Curry, Wax.

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